80. The composition of claim 78, wherein said secondary solvent comprises aqueous lipid emulsion, water, saline solution, dextrose solution, glacial acetic acid, lipid solution or parenteral infusion fluids.--

REMARKS

Status of the Claims:

All the previously pending claims, claims 1-15, 24 and 25, have been cancelled without prejudice or disclaimer. Claims 26-80 have been added. Claims 26-80 are presently pending in the case.

For the convenience of the examiner, the presently pending claims are included herein as **Exhibit A**.

Addition of Claims:

Applicant now elects to prosecute in the present continuation application subject matter described in co-pending Patent Application Serial No. 08/911,607 but not previously claimed. Copending Application Serial No. 08/911,607 describes and presently claims antifungal compositions comprising pimaricin, dipolar aprotic solvent and an aqueous secondary solvent. However, the specification also discloses novel vehicles or "solvent vehicles", and Applicant presently submits claims to compositions comprising the disclosed solvent vehicles. Written support for the term "solvent vehicles" may be found throughout the specification as filed, particularly at page 9, lines 17-18 and at page 18, lines 10-11. Support for the embodiment of the novel solvent vehicles are described throughout the specification and claims as filed, particularly at page 14, lines 22-29:

> The objectives of this experiment were to: (1) design stable pimaricin formulations that are suitable for parenteral administration; (2) establish the chemical and physical stability of pimaricin **in the novel vehicles**; (3) establish the solubility of pimaricin in these vehicles when mixed with NS, dextrose in water, and Intralipid™; and (4) investigate the *in vitro* properties of these

formulations; i.e. their osmolarity, hemolytic potential, and cytotoxicity, to show that they are appropriate for the intended purpose. (emphasis added).

Various specific examples of solvent vehicles are described in the specification as filed, such as at page 16, lines 14-19; at page 17, lines 4-6 and 20-28; at page 19, line 28 to page 20, line 13, including Table 2; at page 21, lines 2-11; at page 23, Table 4 and lines 4-5; and at Figures 6-8. For the convenience of the Examiner, the relevant text, at page 19, line 28 to page 20, line 13, describing examples of various vehicles is shown below:

> It is desirable that a parenteral formulation of a pharmacologically active agent be isosmotic to blood. A hypertonic delivery system can be utilized if the drug/solvent is infused through a (central) venous catheter and gradually diluted in a large blood volume. The osmotic pressure of the various formulations is shown in Table 2.
>
> Table 2
>
> Osmotic Pressures of Various Vehicles with and without Pimaricin

Solution	N	Osmotic pressure mOsm/kg
Water	3	3
Normal saline	3	233
5% dextrose in water	3	286
Blood, human	6	280-295
DMA:PEG:PG	3	4492
Pimaricin in DMA:PEG:PG	3	4732
Intralipid	3	340
DMA:Intralipid (1:10, v/v)	3	2067
Pimaricin in DMA:Intralipid (1:10, v/v, fresh)	3	1930
DMA:Intralipid (1:10, lyophil.-reconstit.)	3	157
Pimaricin (1 mg/ml) in DMA:Intralipid (1:10, lyophil.-reconstit.)	3	208
Pimaricin (25 mg/ml) in DMA:Intralipid (1:10, lyophil.-reconstit.)	3	243

("n" represents the number of independent determinations.)

The DMA-stock formulation with or without pimaricin was very hypertonic; its osmotic pressure was more than 1,900 mOsm/kg, as compared with 280-295 mOsm/Kg for human blood. The DMA/PG/DMSO/PEG and DMA/PEG solvents were almost as hypertonic. In contrast, the DMA/Intralipid preparation was closer to isosmotic when reconstituted after lyophilization. Similarly, the

lyophilized/reconstituted HAc/DMSO/Intralipid™ vehicle was also close to isosmotic. Adding pimaricin to the respective vehicles did not appreciably change their osmolarity ($P > 0.05$).

Specific examples in the novel vehicles, either alone or in combination with other drugs, are also described in the specification as filed, such as at page 9, lines 12-17:

> We have investigated N,N-dimethylacetamide (DMA), DMSO, glycerol, 1,2,-propylene-diol (PG), and polyethylene glycol-400 (PEG) as primary solvents that would be miscible in secondary solvents, examples of which are normal saline, dextrose in water (5% or 10%), and an aqueous soy bean lipid emulsion (Intralipid™). These solvents are examples of vehicles in which pimaricin could be suitably solubilized, yet be safe for human administration, **alone or in combinations with other drugs.** (Emphasis added).

Thus, the disclosures of the solvent vehicles are not limited to those that comprise primaricin, but also include other drug/vehicle combinations, as described at page 19, line 27 to page 20, line 2:

> It is desirable that a parenteral formulation of a **pharmacologically active agent** be isosmotic to blood. A hypertonic delivery system can be utilized if the **drug/solvent** is infused through a (central) venous catheter and gradually diluted in a large blood volume. (Emphasis added).

The novel solvent vehicles can also comprise various other components, as described at page 32, lines 24-25:

> Compositions of the present invention can further include additional pharmaceutically acceptable carriers, adjuvants, and/or biologically active substances.

However, these disclosures of the novel solvent vehicles in combination with other materials are not limited to combinations with an active agent, drug, pharnaceutically acceptable carriers, adjuvants or biologically active substances, as described at page 33, line 8-11:

> The preceding description of specific embodiments of the present invention is not intended to be a complete list of every possible embodiment of the invention. Persons skilled in this field will recognize that modifications can be made to the specific embodiments described here that would be within the scope of the present invention.

Thus, the specification and originally filed claims provides ample written support for the added claims directed to compositions comprising solvent vehicles.

Accordingly, the specification has been amended to at page 1 to give a descriptive title of this aspect of the invention, and at page 2, line 1 to recite the relationship of this application with the parent case, Patent Application Serial No. 08/911,607.

The active claims in this case are claims 26-80.

Claims 26-67 have been added to described the embodiment of the invention, a "solvent vehicle." Support for these claims can be found throughout the specification as filed, with particular support found at page 16, lines 14-19; at page 17, lines 4-6 and 20-28; at page 19, line 28 to page 20, line 13, including Table 2; at page 21, lines 2-11; at page 23, Table 4 and lines 4-5; and at Figures 6-8.

Claims 26-28, 34-35 and 39-43 describe various embodiments of a solvent vehicle. Support for these claims can be found in the specification and claims as originally filed, with particular support found at originally filed claims 1-8 and 20-24; at page 13, lines 25-27, page 15, lines 2-3 and Table 1.

Claims 29-31 and 33 describe embodiments of the aprotic solvent. Support for these claims can be found throughout the specification as filed, with particular support found at page 13, lines 25-27, page 15, lines 2-3 and Table 1.

Claim 32 describe embodiments of the aprotic solvent. Support for this claim can be found throughout the specification as filed, with particular support found at page 9, lines 12-15.

Claim 36 describes an embodiment of an aqueous lipid emulsion. Support for this claim can be found throughout the specification as filed, with particular support found at 13, lines 2-5.

Claim 37 describes an embodiment of an aqueous lipid emulsion. Support for this claim can be found throughout the specification as filed, with particular support found at page 8, lines 21-22,at page 9, lines 12-14 and at page 13, lines 25-27.

Claim 38 describes an embodiment of an aqueous soy bean lipid emulsion. Support for this claim can be found throughout the specification as filed, with particular support found at page 8, lines 21-22,at page 9, lines 12-14 and at page 13, lines 25-27.

Claims 44 and 45 describe embodiments of the dextrose solution. Support for these claims can be found throughout the specification as filed, with particular support found at page 10, lines 19-21 and at page 9, lines 12-15, respectively.

Claim 46 describes an embodiment of the secondary solvent. Support for this claim can be found throughout the specification as filed, with particular support found at page 13, lines 25-28.

Claim 47 describes an embodiment of an aqueous lipid solution. Support for this claim can be found throughout the specification as filed, with particular support found at page 7, line 8 and page 10, line 30.

Claim 48 describes an embodiment of the second solvent. Support for this claim can be found throughout the specification as filed, with particular support found at page 5, lines 19-21 and page 12, line 21 to page 13, line 5.

Claim 49 describes an embodiment wherein the composition further comprises an active agent, drug, pharmaceutical acceptable carriers, adjuvants or biologically active substances. Support for this claim can be found throughout the specification as filed, with particular support found at page 9, lines 12-17; at page 19, line 27 to page 20, line 2; described at page 32, lines 24-25 and at page 33, lines 1-4.

Claims 50-62 describes specific solvent vehicle compositions. Support for these claims can be found throughout the specification as filed, with particular support found at page 6, linse 1-8; at page 7, lines 11-19; at page 17, lines 20-28 and at page 23, lines 4-5 and Table 4; at page 19, line 28 to page 20, line 13, including Table 2; at page 21, lines 2-11; at page 23, Table 4 and lines 4-5; and at Figures 6-8.33-35, 40-45.

Claim 63 describes an embodiment wherein the composition is administered to an animal. Support for this claim can be found throughout the specification as filed, with particular support found at page 10, lines 8-12.

Claim 64 describes an embodiment wherein the composition is administered to a human. Support for this claim can be found throughout the specification as filed, with particular support found at page 10, lines 8-12.

Claim 65 describes an embodiment wherein the composition is administered by parenteral injection. Support for this claim can be found throughout the specification as filed, with particular support found at page 6, lines 5-8.

Claim 66 describes an embodiment wherein the parenterneal injection is intravascular or intraveneous. Support for this claim can be found throughout the specification as filed, with particular support found at page 32, lines 29-30 and at page 6, lines 1-4.

Claim 67 describes an embodiment wherein the composition is administered as an aerosol. Support for this claim can be found throughout the specification as filed, with particular support found at page 32, line 30 to page 33, line 1.

Claim 68 describes an embodiment wherein the composition has been lyophilized. Support for this claim can be found throughout the specification as filed, with particular support found at page 5, lines 12-30.

Independent claim 69 describes an aspect of the invention, wherein the composition comprises a drug, an aprotic solvent and a secondary solvent. Support for this claim can be found throughout the specification as filed, with particular support found at page 5, lines 12-16, at page 19, line 28 to page 20, line 2, and at originally filed claim 17.

Claim 70 describes various embodiments of the aprotic solvent. Support for this claim can be found in the specification and claims as originally filed, with particular support found at originally filed claims 1-8 and 20-24; at page 13, lines 25-27, page 15, lines 2-3, Table 1; and at page 9, lines 12-15.

Claim 71 describes various embodiments of the secondary solvent. Support for this claim can be found throughout the specification as filed, with particular support found at originally filed claims 1-8 and 20-24; at page 13, lines 25-27, page 15, lines 2-3 and Table 1.

Claim 72 describes an embodiment wherein the composition has been lyophilized. Support for this claim can be found throughout the specification as filed, with particular support found at page 5, lines 12-30.

Claim 73 describes an embodiment wherein the composition further comprises a pharmaceutically acceptable aqueous solvent. Support for this claim can be found throughout the specification as filed, with particular support found at page 5, lines 16-18.

Claim 74 describes an embodiment wherein the aqueous solvent is a parenteral infusion fluid. Support for this claim can be found throughout the specification as filed, with particular support found at page 5, lines 19-21.

Claim 75 describes an embodiment of particular types of parenteral infusion fluids. Support for this claim can be found throughout the specification as filed, with particular support found at page 5, lines 19-21.

Claim 76 describes an embodiment of the composition wherein it is suitable for parenteral administration to a mammal. Support for this claim can be found throughout the specification as filed, with particular support found at page 5, lines 16-18.

Claim 77 describes an embodiment wherein the mammal is a human. Support for this claim can be found throughout the specification as filed, with particular support found at page 5, lines 8-9.

Independent claim 78 describes an aspect of the invention, wherein the composition comprises a pharmacologically active agent, an aprotic solvent and a secondary solvent. Support for this claim can be found throughout the specification as filed, with particular support found at page 19, lines 27-28.

Claim 79 describes various embodiments of the aprotic solvent. Support for this claim can be found in the specification and claims as originally filed, with particular support found at originally filed claims 1-8 and 20-24; at page 13, lines 25-27, page 15, lines 2-3, Table 1; and at page 9, lines 12-15.

Claim 80 describes various embodiments of the secondary solvent. Support for this claim can be found in the specification and claims as originally filed, with particular support found at originally filed claims 1-8 and 20-24; at page 13, lines 25-27, page 15, lines 2-3 and Table 1.

It is believed that no fee is due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason, the Assistant Commissioner is authorized to deduct said fees from Arnold White & Durkee Deposit Account No. 01-2508/UTXC:528--1/PAR.

Respectfully submitted,

David L. Parker
Reg. No. 32,165
Attorney for Applicants

ARNOLD, WHITE & DURKEE
P.O. Box 4433
Houston, Texas 77210-4433
(512) 418-3000

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